April 30, 2002

David Brandwene
Akzo Nobel Chemicals Inc.
5 Livingstone Avenue
Dobbs Ferry, New York 10522

Dear Mr. Brandwene:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Butylated Triphenyl Phosphate, posted on the ChemRTK HPV Challenge Program Web site on October 9, 2001. I commend Akzo Nobel Chemicals Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Akzo Nobel Chemicals Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Butylated Triphenyl Phosphate

SUMMARY OF EPA COMMENTS

The sponsor, Akzo Nobel Chemicals Inc., submitted a test plan and robust summaries to EPA dated July 20, 2001, for butylated triphenyl phosphate (CAS# 220352-35-2 (submitter), CAS# 68937-40-6 (TSCA Inventory)). EPA posted the submission on the ChemRTK HPV Challenge Web site on October 9, 2001.

EPA has reviewed this submission and has reached the following conclusions:

1. Test Substance Identification. Because the name and CAS No. do not adequately define this substance, the submitter needs to supply some discussion of the substance identity for the submitted robust summaries as well as all test material used to develop any additional test data. In addition, EPA considers the characterization of the substance in some submitted robust summaries insufficient to determine the adequacy of some endpoints.

2. Physicochemical Data. EPA considers the results for vapor pressure inadequate.

3. Environmental Fate and Pathways. The results for biodegradation appear to be adequate, however the submitter should provide further compositional characterization to sufficiently identity the test substance to allow the adequacy of existing data to be fully assessed.

4. Health Effects. Health effects testing was not proposed by the submitter. The data for acute, repeated-dose, and developmental toxicity are adequate. However, the existing reproductive toxicity data are inadequate and additional testing is suggested. Further, the existing results for genetic toxicity testing are tentatively believed adequate; however, the submitter should provide more detail in the robust summaries to allow the adequacy of existing data to be fully assessed.

5. Ecological Effects. Environmental effects testing was not proposed by the submitter. Upon review of submitted data, EPA tentatively believes the data to be adequate, except that some data elements are missing from the robust summaries. EPA reserves final judgment on the adequacy of these test results pending submission of missing data elements.

EPA requests that the Submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE BUTYLATED TRIPHENYL PHOSPHATE CHALLENGE SUBMISSION

Test Plan

Test Substance Identification

The name of this substance as given by the submitter and the TSCA Chemical Inventory is ambiguous with respect to the number and position of the *t*-butyl substituents. This implies that the substance is a mixture of related chemicals but the test plan does not address this issue or supply information on the production method that could help clarify this point for reviewers. The only related information appears in data summary Section 1.3, which identifies triphenyl phosphate as an impurity in the range of 20-25%. The submitter needs to address chemical identity, by supplying analytical information for typical substance compositions.

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The submitter's approach to these endpoints is acceptable for the purposes of the HPV Challenge Program, except for vapor pressure

The submitter reports a vapor pressure value of 0.13 hPa at 155/C (9.75×10^{-2} torr at 155/C). It is noted that according to OECD Guideline 104, a vapor pressure measurement should be made in the 0 - 50/C temperature range. Because the reported vapor pressure was determined well above 50/C, the data are inadequate for assessment of this endpoint. Furthermore, no reference source or experimental methods are provided. It is not stated in either the test plan or the robust summaries whether the vapor pressure value is for the butylated triphenyl phosphate mixture or for one of the components of the mixture. The submitter needs to provide vapor pressure data for this chemical in the 0 - 50/C temperature range.

The water solubility data reported for butylated triphenyl phosphate appear to be adequate. However, the submitter does not indicate the identity of the test substance. The composition of the test material needs to be clarified for this endpoint.

Environmental Fate (photodegradation, stability in water, biodegradation, and fugacity)

The submitter's approach to these endpoints is acceptable for the purposes of the HPV Challenge Program. However, the submitter needs to provide the composition of the test material used for the biodegradation test.

The experimental biodegradation data reported for butylated triphenyl phosphate appear to be accurate and provide a reasonable assessment of how the substance will degrade in the environment. However, the submitter does not indicate the identity of the test substance. The composition of the test material needs to be clarified before a decision can be made on adequacy.

Health Effects (acute toxicity, repeated-dose toxicity, genetic tonicity, and reproductive/developmental toxicity).

The submitter proposed no additional health effects testing. EPA agrees the data are adequate for the acute, repeated-dose, and developmental toxicity endpoints.

EPA tentatively agrees that existing genetic toxicity data are adequate; however, the submitter should provide more detail in the robust summaries to allow data adequacy to be fully assessed.

The study provided for reproductive toxicity was inadequate to assess butylated triphenyl phosphate. This study that evaluated the effects of hydraulic fluid (the chemical composition of which was not fully described) did report decreased fertility, but this effect could not be clearly ascribed to either butylated triphenyl phosphate or the other components of the fluid. The full chemical composition of this mixture was not reported. Further, the summary lacked discussion of the test method used, including such elements as sample size, control group, and test duration. Therefore, additional reproductive toxicity testing is suggested. Also, there was a discrepancy between the "adequate data" listing for this endpoint in the test plan summary and the rating of "invalid" assigned to the reproductive toxicity study in the summary.

Ecological Effects (fish, daphnia, and algal toxicity).

The submitter proposed no additional environmental effects testing. EPA tentatively agrees adequate data exist for evaluating the acute toxicity to fish, but found deficiencies in the robust summaries for this endpoint. The chronic toxicity to invertebrates summary was also deficient in details necessary to determine if the study is adequate.

Specific Comments on the Robust Summaries

Generic Comments

A full characterization of the composition of the substance tested in individual studies (i.e., provide information on major isomers) is needed in order to determine the adequacy of some endpoints (e.g., biodegradation).

Health Effects.

The summaries generally were adequate, although none of them provided the methods of statistical analyses used in the testing. Also, trade names were sometimes used exclusively; adequate robust summaries must include complete identities and chemical characterizations of test substances.

Acute toxicity. The robust summaries for acute oral (and inhalation) toxicity lack information on control data, the dose tested, and the number of males and females.

Repeated-dose toxicity. The robust summary provided for repeat oral dose toxicity was generally adequate. However, the repeat dose study summary should clarify when cholinesterase activity was measured, as well as how, and where in the body. In addition, data were provided for neurotoxicity. However, the cited studies discuss tests appropriate for assessing delayed neurotoxicity and thus provide supporting data for repeated dose toxicity, but the study summaries lacked some detail, such as test substance characterization.

Genetic toxicity. The robust summaries provided for gene mutation in cultured cells and chromosomal aberration were sufficient to assess the studies, although the dose selection method used in the Ames test was not described. Also, the summary of the Ames test did not include values showing that the test results were negative, and the cytogenetic assay summary lacked numerical values to indicate how cytogenetic responses were measured, and therefore show that test results were negative.

Ecological Effects.

Fish. Both of the robust summaries for acute fish toxicity were missing information. Specifically, the 1979 study summary lacked the following details: the number of fish exposed per concentration, the number of replicates, chemical purity, pH, DO, temperature, and water hardness. The 1996 study was not considered a key study because the results did not meet the OECD limit test.

Invertebrates. Missing data elements from the robust summary for acute invertebrate toxicity include: water hardness, number of organisms per concentration, number of replicates, chemical purity, pH, DO, and temperature.

Algae. The following data elements for acute algal toxicity should be submitted: pH, temperature, water hardness, chemical identification and purity, GLP indication, test year, methods used, and endpoints assessed.

Daphnid Chronic. Missing data elements from the robust summary for chronic daphnid toxicity include the following: study guideline type, test type, water hardness, pH, temperature, DO, chemical purity, and survival and reproductive tables to determine how much a reduction in deaths occurred, or an EC50 value for reproduction.

References

Reference Number 6 of the test plan is incorrect, Latendresse et al. was published in 1994 rather than 1993.

Followup Activity

EPA requests that the Submitter advise the Agency within 60 days of any modifications to its submission.